REMARKS/ARGUMENTS

Claims 39-55 are active. Claims 39-51 are method of detection claims; claims 52-54 are product (protein chip) claims. Claims 1-38 have been withdrawn from consideration and have now been cancelled without prejudice to their presentation in a Divisional Application.

Independent claim 39 finds support at page 20, lines 9-14 and in original claims 28 and 29, which describe detection of autoantibodies in the serum of an individual; and on page 19, lines 26-34 and by original claims 24 and 25 which describe ZnT-8 and its fragments. Antigen-antibody complex formation is well-known in the art and is also described between ZnT-8 protein and antibodies to ZnT-8 on page 15, lines 14-20. Protein chips of claims 49-54 are disclosed on page 19, line 38-page 20, line 8 and in original claim 26. Claim 55 is a variant of claim 39 comprising the same steps in the body of the claim, but a preamble which refers to the detection of serum autoantibodies to ZnT-8. In view of the above, the Applicants submit that no new matter has been introduced. Favorable consideration of this Amendment and allowance of this application is respectfully requested.

The Applicants thank Examiner Ewoldt for the courteous and helpful interview of May 14, 2009. The Applicants believe that agreement was reached regarding actions which would remove the drawing objection and the indefiniteness rejection. The enablement and lack-of-description rejections were reviewed. The Applicants pointed out that SEQ ID NOS: 2 and 7-10, respectively describe the ZnT-8 sequence and particular domains of ZnT-8 (paragraph bridging pages 23-24). Information showing that diabetic subjects have higher levels of autoantibodies to ZnT-8 was revised. To help overcome these rejections, the Applicants were encouraged to simplify the claim language and further substantiate the nexus between higher levels of ZnT-8 autoantibodies and diabetes, for example, by submission of scientific articles or by filing a Declaration showing such a nexus.

Objection--Drawings

This objection is moot in view of the attached Replacement Drawings.

Rejection—35 U.S.C. §112, first paragraph

Claims 39-46 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate enablement for a method of detecting autoantibodies to ZnT-8 and whether autoantibodies to ZnT-8 if detected correlated with diabetes. To simply prosecution and avoid certain enablement issues, the claim language has been simplified, for example, by eliminating the term "specifically targeting the beta cells" and by directing the claims to ZnT-8 and its fragments instead of to particular fragments.

Page 20, lines 9-14 and original claims 28 and 29 describe detection of autoantibodies in the serum of an individual using ZnT-8 and its fragments, which are further described on page 19, lines 26-34 and by original claims 24 and 25.

As shown by *Wenzlau, et al.*, PNAS 104:17040 (2007), ZnT-8 is a major autoantigen in human type 1 diabetes and type I diabetes "results from progressive loss of pancreatic islet mass through autoimmunity" (abstract). ZnT-8 "was targeted by autoantibodies in 60-80% of new-onset T1D compared with < 2% of controls" (abstract).

Wenzlau, et al., Curr. Opin. Endocrinol. Diabetes Obes. 15:315 states "Initial epitope mapping of ZnT-8 autoantibodies (ZnT8A) in newly diagnosed T1D patients showed that up to 70% of individuals had antibodies reactive to the carboxy terminal 102aa (C-term; aa 268-369) and 10% to the amino terminal 74 aa". These attached documents show that the claimed methods were enabled by substantiating that ZnT-8 and its fragments actually identify autoantibodies from type I diabetes subjects. Therefore, in view of the amendments above and the documentary evidence of record showing that autoantibodies to ZnT-8 correlated with subjects having type I diabetes, this rejection may now be withdrawn.

Rejection—35 U.S.C. §112, first paragraph

Claims 39-46 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. The Applicants believe that this rejection is moot in view of the amended claim language above which deletes "specifically targeting the β cells" and the descriptive support indicated above, for example, at page 20, lines 9-14 and in original claims 28 and 29, which describe detection of autoantibodies in the serum of an individual. The correlation between autoantibodies to pancreatic antigens and Type 1 diabetes was well-known as of the filing date of this application as shown for example by *Batstra, et al.*, Clin. Lab. 47:497 (2001), "Prediction and Diagnosis of Type 1 Diabetes Using β-cell Autoantibodies", *Kukreja, et al.*, J. Clin. Endocrinol. Metabol. 84:4371, "Autoimmunity and Diabetes", and as detailed in the Declarations of record by Dr. Favier and Dr. Seve which describe autoimmune β-cell destruction as a "crucial event" at onset of diabetes (Cell 85:291; Nature: 414:792). This correlation is now explicitly mentioned in the last phrases of independent claims 39 and 55. A patent specification need not teach, and preferably omits, what is well known in the art *Hybritech Inc. v. Monoclonal Antibodies*, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). In view of the above disclosure and what was well-known in the art (as well as the claim language amendments), the Applicants respectfully submit that this rejection no longer applies and cannot be sustained.

Rejection—35 U.S.C. §112, second paragraph

Claims 39-48 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the adoption of the revision kindly suggested by the Examiner.

Conclusion

This application presents allowable subject matter and the Examiner is respectfully requested to pass it to issue. The Examiner is kindly invited to contact the undersigned should a further discussion of the issues or claims be helpful.

Respectfully submitted,

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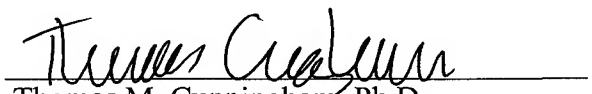

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